NEPHROLOGY

ACUTE KIDNEY INJURY

1) Increase serum creatinine by 0.3 mg/dL (26.5umol/L) within 48 hours
2) 1.5 fold increase over baseline within the past 7 days
3) Oliguria (Urine output < 0.5ml/kg/hour) for at least 6 hours

PRE-RENAL AKI

Definition: Real/effective decrease in GFR due to hemodynamic changes.

Causes:

A) volume depletion (blood loss/hypotension/diuretics)
B) HF
C) **Drugs** (afferent vasoconstriction):
  - NSAIDS (Block Prostaglandins which provide vasodilation)
  - Calcineurin inhibitors (Cyclosporin/Tacrolimus)
D) **Drugs** (efferent vasodilation):
  - ACEIs/ARBs
E) **Hepatorenal Syndrome**
  - Clues: Ascites/Esophageal varices/Spleenomegaly/jaundice)
F) **Compartment Syndrome**
  - Causes: Trauma, Intraperitoneal Bleeding, Pancreatitis
  - AKI occurs 2ry to renal vein compression
  - Dx: Manometry >> Intra-abdominal pressure > 20 mmHg
  - Rx: Surgical Decompression / High volume paracentesis

LAB:

A) BUN:Cr ratio: > 20:1
B) **Urine Osmolality:** > 400 mOsm
C) Urine Na: < 20 mEq
D) Urine FEna < 1% (not reliable in patients on Diuretics)
E) Urine FEurea < 35%
F) Urine FEuric acid < 12%
G) **Urine Microscopy:** Granular casts, Hyaline casts

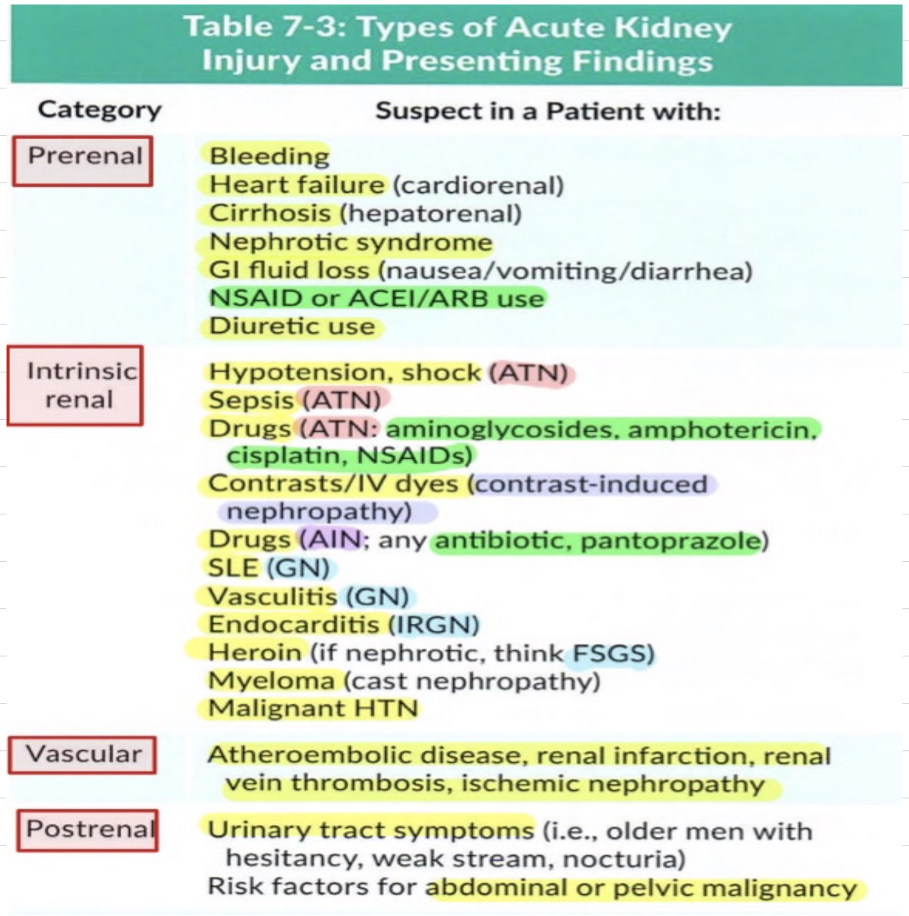


Table 7-3: Types of Acute Kidney Injury and Presenting Findings

Category	Suspect in a Patient with:
Prerenal	Bleeding Heart failure (cardiorenal) Cirrhosis (hepatorenal) Nephrotic syndrome GI fluid loss (nausea/vomiting/diarrhea) NSAID or ACEI/ARB use Diuretic use
Intrinsic renal	Hypotension, shock (ATN) Sepsis (ATN) Drugs (ATN: aminoglycosides, amphotericin, cisplatin, NSAIDs) Contrasts/IV dyes (contrast-induced nephropathy) Drugs (AIN; any antibiotic, pantoprazole) SLE (GN) Vasculitis (GN) Endocarditis (IRGN) Heroin (if nephrotic, think FSGS) Myeloma (cast nephropathy) Malignant HTN
Vascular	Atheroembolic disease, renal infarction, renal vein thrombosis, ischemic nephropathy
Postrenal	Urinary tract symptoms (i.e., older men with hesitancy, weak stream, nocturia) Risk factors for abdominal or pelvic malignancy

INTRINSIC

ACUTE TUBULAR NECROSIS

- Most common cause of Intrinsic AKI
- Tubular dysfunction is the hallmark of ATN
- The reduction of GFR usually persist for 1-2 weeks

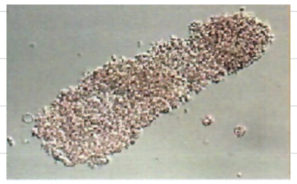
CAUSES:

A) Ischemic ATN:
  - Most common form of ATN, occurs in any form of shock

B) Nephrotoxic ATN:
- Myoglobin (Rhabdomyolysis)
  Causes: Crush injuries, Seizures, Heat strokes, Malignant Hyperthermia
  LAB: Hyperkalemia/ Hyperphosphatemia/ Hyperuricemia/ Hypocalcemia
  Rx: Aggressive Isotonic fluid resuscitation Target urine output 3ml/kg
- Free Hgb (Intravascular hemolysis).
  Rx: Similar to Myoglobin induced Nephropathy
- Contrast induced Nephropathy: Occurs 24-48 hours after exposure
  Prevent with: IV NS before and after contrast exosure
- Uric Acid (Tumor lysis Syndrome)
- Osmotic Nephropathy: (IVIG with sucrose, Mannitol, Dextran)
- **Acute phosphate Nephropathy:** Bowel preparation containing sodium phosphate
  Risk factors: 1) GFR < 60 2) Advanced age 3) Dehydration 4) DM 5) HTN 6) ACE/ARB

Diagnosis: Hyperphosphatemia out of proportion to the degree of kidney injury
- **Drugs:** NSAIDs/ Amphotericin B/ Aminoglycoside/Cisplatin/ Cidofovir/ Tenofovir/ Foscarnet
  NOTE: Correct Hypokalemia or Hypomagnesemia prior to Aminoglycoside treatment to decrease risk of nephrotoxicity

LAB: (NOTE: if severe volume depletion is the cause of ATN, it can Present like Pre-renal AKI)



A) BUN:Cr ratio 10:1 to 15:1
B) Urine osmolality < 350
C) Urine Na > 40
D) Urine FEna > 2%
E) Urine FEurea > 50%
F) **Urine Microscopy: Granular casts/ Muddy brown casts**

ACUTE INTERSTITIAL NEPHRITIS

- Most often Drug induced Hypersensitivity reaction
- Fever/ Eosinophilia/ Eosinophilurea/ Rash

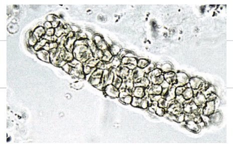
CAUSES:

A) **Medication:**
- NSAIDS >> Can Cause similar presentation to Minimal change disease with nephrotic range proteinuria
- PPI
- Allopurinol
- Cimetidine
- Thiazide
- Cimetidine
- Antibiotics (β lactams/ Bactrim/ Rifampin/ Ciprofloxacin)

B) **Infection** (Pyelonephritis/ Legionella/ Streptococci/TB)
C) **Diseases** (SLE/ Sjogren/ Sarcoidosis)
D) **Heavy metals** (Usually cause Chronic Interstitial Nephritis)
E) **Transplant rejection**

LABORATORIES:

A) Diagnosis: Renal Biopsy
B) Urine FEna > 1%
C) urine Na > 20
D) **Urine Microscopy:** RBC, WBC, Eosinophiluria, WBC Cast (Sterile Pyuria)
E) Eosinophilia



MANAGEMENT:

- Discontinuing the offending agents
- Steroids

Post-renal AKI (Obstructive Uropathy)

Upper Urinary Tract Obstruction:

- Anywhere upstream of the Ureterovesical junction
- Causes:
  a) Kidney Stones
  b) Drugs (Crystal induced): Methotraxate/Indinavir/Acyclovir/Sulfa antibiotics
  c) Papillary Necrosis:
    - Severe Pyelonephritis/Chronic analgesic abuse/ SCD
    - U/A: Sterile Pyuria
  d) Retroperitoneal Fibrosis:
    - Inflammation and fibrosis in the retroperitonium that can encase and obstruct the ureters
    - Present with: Back pain, Weigh loss, Fatigue
    - IgG4 related disease (Review in Rheumatology!)
  e) Anatomic Anomalies

Lower Urinary Tract Obstruction (Urinary Retention)

- Patients may have suprapubic pain from the distended bladder
- Causes:
  a) BPH: nocturia/frequency/hesitancy/weak stream/incomplete voiding
  b) GU Malignancy
  c) Stones
  d) Urethral Stenosis
  e) Urethral stricture
  f) Medication:
    - Antichlinergic (Oxybutynin/Dicyclomine)
    - Sympathomimetics (Phenylephrine/Psuedoephedrine)
    - Antihistamines (Diphenhydramine)
    - Psychiatric medication (Haloperidol/Amitriptyline)

Work Up

A) **Urine Microscopy:** Bland wit no Abnormalities
B) **Upper UT Obtruction:** U/S or CT
C) **Lower UT Obstruction:** Bedside Bladder U/S or Postvoid residual measurements

Treatment:

- Resolve the obstruction

$$\mathrm{FE_{Na}}\,(\%) = \frac{(\mathrm{S_{Cr}} \times \mathrm{U_{Na}}) \times 100}{\mathrm{S_{Na}} \times \mathrm{U_{Cr}}}$$

$$\mathrm{FE_{Urea}}\,(\%) = \frac{(\mathrm{S_{Cr}} \times \mathrm{U_{Urea}}) \times 100}{\mathrm{BUN} \times \mathrm{U_{Cr}}}$$

1.A 27-year-old man comes to the physician because of a 10-day history of crampy lower abdominal pain and diarrhea that awakens him at night. He says he might have some blood in his stool, but he is not sure. He also complains of fatigue. His past medical history is unremarkable. He takes a daily multivitamin and exercises regularly. He has a stable male partner and uses condoms regularly. His mother died of lymphoma and his older brother suffers from ulcerative colitis.

He is afebrile. His blood pressure is 130/88 mm Hg, pulse is 90/min, and respirations are 12/min. His bowel sounds are normoactive. There is mild abdominal tenderness in both lower quadrants without rebound tenderness. His examination is otherwise unremarkable. The patient's labs reveal:

Hematocrit	24%
MCV	87 fl
Platelets	55,000 cells/µL
Leukocyte count	11,000 cells/µL
Sodium	140 mEq/L
Potassium	4.4 mEq/L
Chloride	102 mEq/L
Bicarbonate	22 mEq/L
Creatinine	2.4 mg/dL

Which of the following is the best next step in managing this patient?

A. Antimotility drugs

B. Peripheral blood smear

C. Empiric antibiotics

D. Sigmoidoscopy

E. Stool cultures

2. A 67-year-old woman is evaluated prior to angiography for intermittent claudication. At a recent evaluation, her ankle-brachial index was 0.65 on the right and 0.75 on the left. She has a history of long-term cigarette smoking, hypertension, type 2 diabetes mellitus, severe degenerative arthritis of her knees, and hyperlipidemia. Current medications include simvastatin, ibuprofen, glipizide, and amlodipine.

Her blood pressure is 130/86 mm Hg and pulse is 72/min. Cardiac exam reveals a grade 2/6 systolic ejection murmur at the base. Her lungs are clear and there is no jugular venous distension. Her tibial pulses are 1+ and she has trace pedal edema to the ankles bilaterally.

Her creatinine level is 2 mg/dL and urinalysis shows 2+ proteinuria.

In addition to using the smallest dose of a third generation contrast agent and pre-hydration with normal saline, which of the following should be done?

A. Discontinue ibuprofen

B. Furosemide during and post-procedure

C. Intravenous dopamine during the procedure

D. Mannitol pre- and intra-procedure

E. Prophylactic hemofiltration

7. A 65-year-old man is brought to the emergency department with a 48-hour-history of fever, lethargy, and a hacking cough. On the morning of admission, his wife found him in a severe state of confusion in bed. He had some incontinence during the night and had wet the bed and soiled the sheets. The patient was very sleepy in the ambulance on the way to the hospital. He has type 2 diabetes mellitus, hypertension, hyperlipidemia, and benign prostatic hyperplasia. Current medications include chlorthalidone, simvastatin, indapamide, metformin, and finasteride. He has no known drug allergies.

On examination, he appears acutely ill. His temperature is 39.7 C (103.5 F), blood pressure is 152/84 mm Hg, pulse is 90/min, and respirations are 18/min. The patient's pulse oximetry shows 95% at room air. Mucous membranes are moist. Rales are heard at the right lung base on auscultation. There is mild resistance to neck flexion. Laboratory studies are as follows:

Complete blood count	
Hematocrit	44%
Leukocytes	14,000/mm3
Serum chemistry	
Sodium	136 mEq/L
Potassium	4.9 mEq/L ↑
Chloride	102 mEq/L
Bicarbonate	22 mEq/L
Blood urea nitrogen	18 mg/dL
Creatinine	2 mg/dL
Calcium	8.4 mg/dL ↓ (8·6-10·3)
Glucose	160 mg/dL
Phosphorus, inorganic, serum	6.0 mg/dL
Uric acid, serum	10 mg/dL ↑(3·5-7·2)
Albumin	4.0 mg/dL
Urinalysis	
Specific gravity	1.025
Blood	gross
Protein	2+
Nitrites	negative
White blood cells	1-2/hpf
Red blood cells	1-2/hpf

The urinary fractional excretion of sodium (FENa) is calculated at 0.8%. A chest x-ray reveals a right lower lobe pneumonia. He receives 500 mL of intravenous normal saline, ceftriaxone, and azithromycin.

Which of the following is the most likely cause of this patient's acute kidney injury?

A. Interstitial nephritis

B. Lactic acidosis

C. Pigment induced kidney injury

D. Uric acid nephropathy

E. Volume depletion

4. A 40-year-old construction worker is brought to the emergency department. He was involved in a demolition accident and was trapped for 7 hours under a large piece of concrete that fell across both thighs. He is alert and conscious and says he is in otherwise good health. He takes no medications.

His blood pressure is 100/70 mm Hg, pulse is 90/min, and respirations are 20/min. Pulse oximetry is 98% on room air. He is afebrile. His general physical examination is within normal limits except for evidence of extensive crush injury involving both thighs. Peripheral pulses are 2+ and deep tendon ankle reflexes are 2+ bilaterally.

Stat laboratory work is pending. A bladder catheter reveals 20 mL of dark urine that is positive for blood.

Which of the following is the best initial therapy for this patient?

A. Isotonic bicarbonate solution

B. Mannitol

C. Normal saline

D. Normal saline and oral acetylcysteine

E. Ringer's lactate

3. A 60-year-old man with recently diagnosed advanced stage diffuse large B cell lymphoma was treated with combination chemotherapy. Thirty-six hours prior to treatment, he was given intravenous normal saline at 200 ml/hour and 600 mg of allopurinol.

His temperature is 37.0 C (98.6 F), blood pressure is 128/84 mm Hg, pulse is 84/min, and respirations are 18/min. He has bulky diffuse lymphadenopathy and splenomegaly. Cardiac and lung examinations are within normal limits. There is no peripheral edema. His current urine output is 10 ml/hr.

The patient's labs reveal:

Complete blood count	
Hematocrit	33%
Platelets	152,000/µL
Leukocyte count	6,100/µL
Serum chemistry	
Sodium	140 mEq/L
Potassium	5.9 mEq/L ↑
Chloride	100 mEq/L
Bicarbonate	22 mEq/L
Creatinine	3.0 mg/dL ↑
Calcium	8.1 mg/dL (8·6 - 10·3) ↓
Blood glucose	130 mg/dL
Phosphorus, inorganic	10.0 mg/dL
Uric acid	14.5 mg/dL (3·5- 7·2) ↑
Urine	
Specific gravity	1.015
Blood	negative
Protein	trace
WBC	1-2/hpf
RBC	1-2/hpf
Casts	many hyaline and finely granular
Crystals	none

Which of the following is the best next step in treating this patient?

A. Acetazolamide

B. Allopurinol

C. Febuxostat

D. Hemodialysis

E. Rasburicase

7. A 39-year-old man is admitted to the hospital for acute alcoholic pancreatitis. His initial APACHE II score was 20, suggestive of severe disease. Within the first 48 hours, he received a total of 10 liters of intravenous fluid resuscitation. Because of decreasing oxygenation, he was intubated and started on mechanical ventilation. Due to increased oxygen requirements, both PEEP and FiO2 were progressively increased. Over the past 12 hours, his urine output decreased and his serum creatinine increased from 1.2 mg/dL at admission to 2.2 mg/dL at present.

His blood pressure is 110/70 mm Hg and pulse is 98/min. Jugular venous pressure is elevated. Lung examination reveals bilateral crackles at the lung bases. His abdomen is diffusely tender and tensely distended. Bowel sounds are diminished. There are no flank or periumbilical ecchymoses. There is 3+ pitting edema to mid-thighs bilaterally. Urinalysis results are as follows:

Specific gravity	1.015
Protein	none
Blood	negative
Leukocyte esterase	negative
Nitrites	negative
White blood cells	0-5/hpf
Red blood cells	0-5/hpf

Which of the following would most likely establish the cause of the acute kidney injury?

A. Abdominal CT scan

B. Fractional excretion of sodium

C. Measurement of bladder pressure

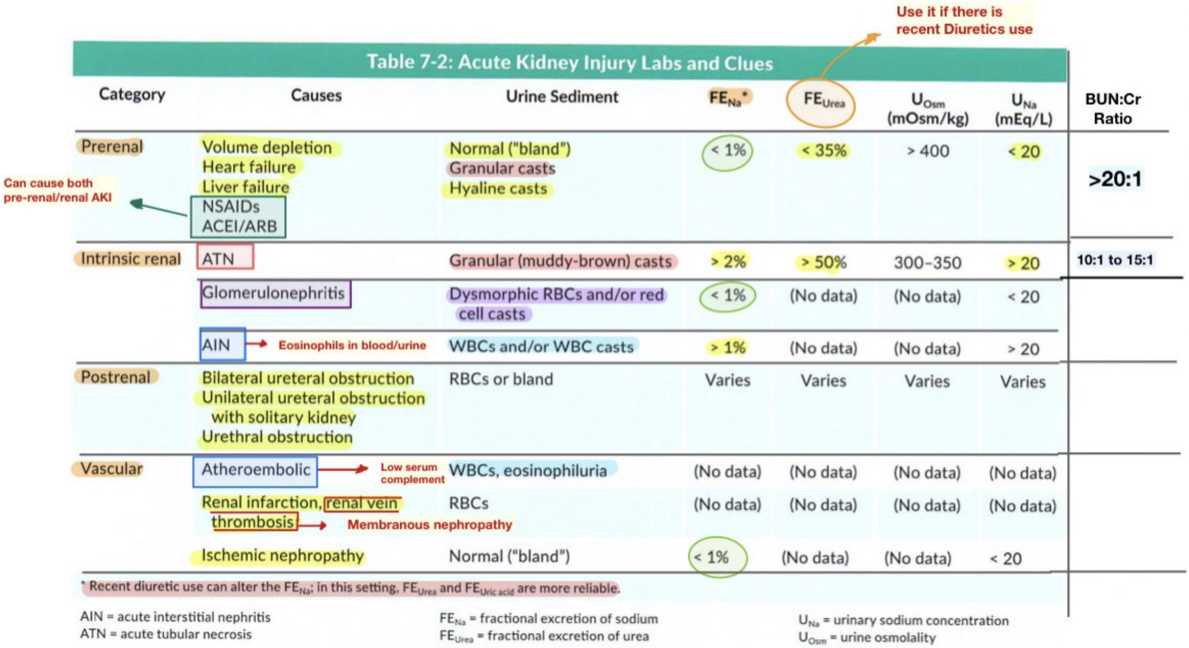
D. Renal ultrasound

E. Serum complement levels

TLS Likelihood	**Preferred Treatment**
Low	Aggressive IV fluids and monitoring
Intermediate	Allopurinol if serum uric acid < 8 mg/dL+ IVF **or** Rasburicase if serum uric acid > 8 mg/dL + IVF
High	Rasburicase
Established TLS	Hemodialysis

Laboratory features of rhabdomyolysis

Muscle enzymes	• Elevated CK (often >10,000 U/L)
Urine tests	• Red to brown urine with positive blood but no RBC (myoglobinuria)
Electrolytes	• Hyperkalemia, hyperphosphatemia & hyperuricemia due to intracellular electrolyte release • Hypocalcemia & dehydration due to influx of calcium & intravascular fluid into injured muscles
Creatinine	• AKI due to tubular injury from myoglobinuria • FENa can be falsely low



Use it if there is recent Diuretics use

Table 7-2: Acute Kidney Injury Labs and Clues

Category	Causes	Urine Sediment	FE_{Na}*	FE_{Urea}	U_{Osm} (mOsm/kg)	U_{Na} (mEq/L)	BUN:Cr Ratio
Prerenal	Volume depletion Heart failure Liver failure NSAIDs ACEI/ARB	Normal ("bland") Granular casts Hyaline casts	< 1%	< 35%	> 400	< 20	>20:1
Intrinsic renal	ATN	Granular (muddy-brown) casts	> 2%	> 50%	300–350	> 20	10:1 to 15:1
	Glomerulonephritis	Dysmorphic RBCs and/or red cell casts	< 1%	(No data)	(No data)	< 20	
	AIN → Eosinophils in blood/urine	WBCs and/or WBC casts	> 1%	(No data)	(No data)	> 20	
Postrenal	Bilateral ureteral obstruction Unilateral ureteral obstruction with solitary kidney Urethral obstruction	RBCs or bland	Varies	Varies	Varies	Varies	
Vascular	Atheroembolic → Low serum complement	WBCs, eosinophiluria	(No data)	(No data)	(No data)	(No data)	
	Renal infarction, renal vein thrombosis → Membranous nephropathy	RBCs	(No data)	(No data)	(No data)	(No data)	
	Ischemic nephropathy	Normal ("bland")	< 1%	(No data)	(No data)	< 20	

Can cause both pre-renal/renal AKI

* Recent diuretic use can alter the FE_{Na}; in this setting, FE_{Urea} and $FE_{Uric\ acid}$ are more reliable.

AIN = acute interstitial nephritis
ATN = acute tubular necrosis

FE_{Na} = fractional excretion of sodium
FE_{Urea} = fractional excretion of urea

U_{Na} = urinary sodium concentration
U_{Osm} = urine osmolality

NEPHROTIC SYNDROMES:

Defined as:

1) Absence of Inflammation
2) Nephrotic range Proteinuria (> 3.5 gm/day)
3) Hypoalbuminemia
4) Edema

Workup:

Urine microscopy + Sediment
Spot urine Protein/Cr ratio
Anti dsDNA, C3/C4, HBV/HCV, HIV, SPEP/ UPEP CA Screen
APA2R Antibodies, HbA1C/ Fundoscopy for Retinopathy

NOTE:

Biopsy should be done in all cases of nephrotic syndrome when the underlying cause is not obvious

Presentation:

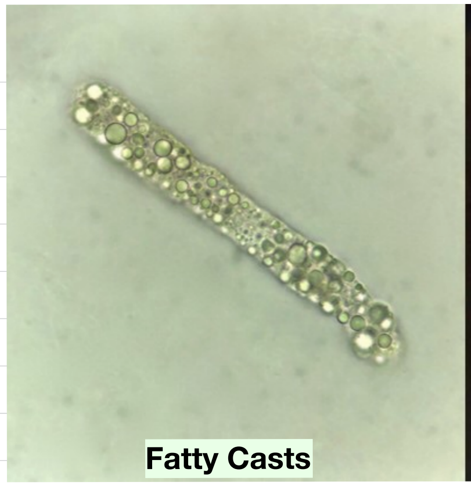
A) Frequent infections (especially Hemophilus influenzae and streptococcus pneumoniae : From the urinary loss of Immunoglobulins
B) Hypercoaguable state: From the urinary loss of Antithrombin III
C) Hyperlipidemia

Syndromes:

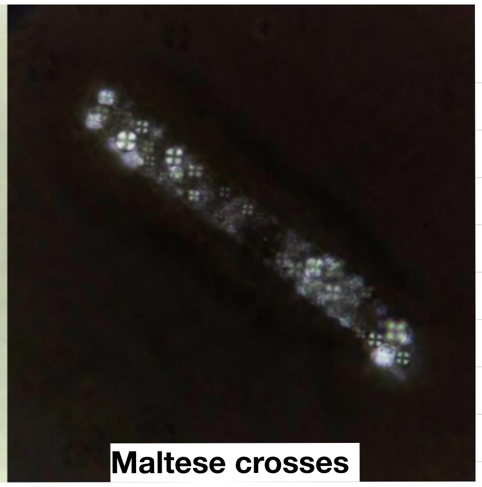
1) MCD
2) Membranous Nephropathy
3) FSGS
4) MPGN
5) Amyloidosis
6) Diabetic nephropathy

Urine sediment:

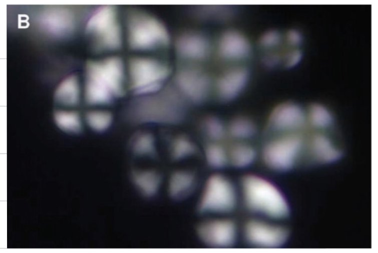
- Fatty Casts / Oval fat bodies / Maltese Crosses



Fatty Casts



Maltese crosses



Maltese crosses

NOTE: **Seen More with MCD**

MINIMAL CHANGE DISEASE (MCD)

Most common cause of 1ry Nephrotic syndrome in children

SECONDARY CAUSES

A) Drugs: NSAIDS / Lithium / Ampicillin
B) Diseases: Lymphoma (Hodgkin > Non Hodgkin) / SLE / DM/ Celiac disease

PRESENTATION

- Anasarca
- severe Peripheral edema
- Usually DOES NOT PRESENT WITH HTN
- **Urine Microscopy:** Fatty Casts / Oval fat bodies (Maltaese crosses under polarized light)
- **Light Microscopy:** Normal Histology (that is why it's called minimal change)
- **Electron Microscopy:** **Fusion of epithelial podocytes foot processes**

TREATMENT:

- Steroids
- Cyclophosphamide / Cyclosporine (for steroid dependent or steroid resistant disease)

DIABETIC NEPHROPATHY

- Most Common Cause of Systemic (2ry) of Nephrotic Syndrome in Adults
- Most Common Cause of ESRD Worldwide
- Can Cause RTA Type 4
- Retinopathy usually Precedes Nephropathy

RISK FACTORS

- Family Hx of ESRD
- African American / Hispanic
- Uncontrolled HTN
- Poor Glycemic control
- Obesity
- Smoking

PATHOPHYSIOLOGY

1) Nodular GlomerularSclerosis (Kimmelstiel wilson lesion)
2) Hyperfiltraton (increased GFR)
3) MICROalbunminuria (not detected by dipstick)
4) MACROalbuminuria (Positive in dipstick)
5) Nephrotic Range Protienuria

TREATMENT

A) ACEs/ARBs (if moderately increased Albuminuria) Even if Normotensive
B) Control HTN
C) Glycemic control
D) Weight Reduction
E) treat Hyperlipidemia
F) SGLT2 Inhibitors (Should not be used in patient with eGFR < 30)

MEMBRANOUS NEPHROPATHY

PRIMARY (IDIOPATHIC(

- Most common cause of Nephrotic Syndromes in Adults
- Especially Caucasian males > 40 years of age
- Positive Antiphospholipase A2 receptor (Anti-PLA2R) antibodies

SECONDARY

- Solid tumors (breast/ Colon/ Lung/ Blasdder)
- Infections: Hepatitis (**HBV > HCV**) / Malaria / Syphilis / Schistosomiasis
- Drugs: Captopril / Gold / NSAIDS / Anti TNF agents / Penicillamine
- Autoimmune: SLE (Class 5)/ Rheumatoid arthritis / Thyroiditis

PRESENTATION

- Nephrotic Syndrome
- Most patients have Norma Blood Pressure and Renal function at diagnosis
- Highest Prevalence of Renal Vein Thrombosis compared to other syndromes

Flank pain, Hematuria, High LDH, think about Renal infarction from Renal Vein thrombosis

Microscopic Findings:

- Light Microscopy:
  - -Thickened capillary walls
  - Spikes and Domes appearance of Basement membrane
  - IgG and C3 Deposits on Immunofluorescence
- Electron Microscopy:
  - Subepithelial Electron dense deposits

TREATMENT

Primary: *Can have Spontaneous remission (not all patients need to be treated)*

- Conservative : ACEs/ARBs, and HTN Control
- Persistant proteinurea (>4gm/day) Steroids / Rituximab/ Cyclophospamide

Secondary: Treat underlying disease or Discontinuation of offending drugs

FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS)

- Most common Cause of Idiopathic Nephrotic Syndrome in African
- In African: Associated with the APOL1 gene variant
- can recur after Kidney Transplantation

SECONDARY CAUSES

- HIV/AIDS: Collapsing Variant FSGS (a.k.a HIV Associated nephropathy), which can progress rapidly to ESRD
- Heroin Use
- Obesity
- Sickle Cell Disease
- Reduced renal Mass
- Chronic Vesicoureteral reflux
- Medication: Bisphosphonates / Anabolic steroids/ Interferon / Cyclosporine

PRESENTATION Nephrotic Syndrome + HTN

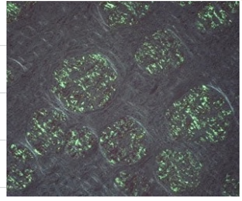
ELECTRON MICROSCOPY: Diffuse Foot Processes Fusion

TREATMENT

1ry: ACEs/ARBs And High Dose Steroids
2ry: ACEs/ARBs + treat underlying cause

NOTE
Initiate Antiretroviral Therapy in all Patients with HIV Associated nephropathy

AMYLOIDOSIS



PRIMARY (Immunoglobulin light chain [AL] Amyloidosis)

- Can occur alone or associated with Multiple Myeloma
- Multi system disease

SECONDARY (Amyloid A [AA] Amyloidosis)

- Seen in chronic Inflammatory states (Rheumatoid arthritis/FMF)
- Can cause: (Carpal tunnel syndrome, Heart failure, Nephrotic syndrome)

Congo red Stain : Apple green birefringence under polarized light
NOTE: Can Cause Enlarged kidney Size

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS (MPGN)

COMPLEMENT MEDIATED MPGN:

- Immune Fluorescence is positive for Complement but negative for Immunoglobulin
- due to Dysregulation of the Alternative Complement pathway by Either:

1) Genetic mutation to complement regulatory proteins
   Rx: Intermittent FFP Infusion
2) Antibodies against Complement regulatory proteins
   Rx: Plasma Exchange / Eculizumab

- Low C4 and C3. → Stays low Indefinitely

IMMUNE COMPLEX MEDIATED MPGN:

- Immune Fluorescence is Positive for Complement (C3) and Immunoglobulin
- Usually due to Underlying Systemic Disease:

Can Present as both Nephrotic and nephritis Syndromes

A) Chronic Infection:
  - Hepatitis (**HCV > HBV**)
  - NOTE: Hepatitis C is the most common Cause
  - Shunt nephritis
  - Abscess

B) Cryoglobulinemia:
  - Can be Caused by Hepatitis C
    Rx: Steroids, Plasmapheresis, Rituximab / Cyclophosphamide

C) Autoimmune
  - SLE
  - Sjogren Syndrome

D) Monoclonal Gammopathy

TREATMENT

- Treat the underlying disease

NEPHROTIC SYNDROME RAPIS REVIEW

TABLE 12.8. Primary Causes of Nephrotic Syndrome

DISEASE	PRESENTATION	TREATMENT	CLINICAL COURSE
Minimal change disease	Sudden onset with heavy proteinuria More common in children Associated with atopic disease NSAIDs Lymphoma	Steroids	Responds to steroids but often relapses Renal failure is uncommon
Focal segmental glomerulosclerosis	↑ in African Americans (APoL 1 Gene) HIV/Black/obesity SCD	Steroids, cyclosporine; cyclophosphamide	Up to 50% develop ESRD within 5 years
Membranous nephropathy	Predilection to clotting—renal vein thrombosis Most common in Adults Solid Tumors / Whites HBV > HBC	Observation with ACEIs/ARBs if slow progression Steroids; cyclosporine, tacrolimus, mycophenolate	Twenty-five percent spontaneously remit **"1/3 get better, 1/3 stay the same, 1/3 get worse"** Slow progression to renal failure
MPGN	Can present with either nephritic or nephrotic features Associated with HCV/cryoglobulins, HBV, HCV, subacute bacterial endocarditis, syphilis; autoimmune (SLE, Sjögren); malignancy	**Non-nephrotic: Observe** **Nephrotic or worsening renal function: Steroids** HCV > HBV	Fifty percent die or progress to ESRD within 5 years of renal biopsy

TABLE 12.9. Systemic Diseases That Cause Nephrotic Syndrome

DISEASE	PRESENTATION	TREATMENT	CLINICAL COURSE	NOTES
Diabetic nephropathy	Onset 5-10 years after diagnosis in type 1 DM; more variable in type 2 **High prevalence of simultaneous DM retinopathy**	Glycemic control Target LDL <100 mg/dL Target BP <130/80 mm Hg **ACEIs/ARBs are first-line treatment**	Progresses from hyperfiltration to microalbuminuria to nephrotic to ESRD	The leading cause of ESRD in the United States BP control is very important in slowing GFR decline
Multiple myeloma	**More severe renal failure with cast nephropathy** May have tubular dysfunction, **Fanconi syndrome** (glycosuria, aminoaciduria, phosphaturia, bicarbonaturia)	See the Hematology chapter	Higher creatinine is correlated with worse survival Survival improves if stem cell transplantation is successful	Monoclonal gammopathy on SPEP/UPEP **Light chains will not be detected by urine dipstick for protein**
Amyloidosis	May have heavy proteinuria of >20 g/day **AL (1°): *Amyloid* Ig *Light* chain** deposition; associated with multiple myeloma/MGUS **AA (2°):** Serum ***Amyloid A*** protein deposition; associated with **chronic inflammation and infection**	**AL:** See the Hematology chapter **AA:** Control the underlying condition	Mean survival in 1° amyloidosis is months	

GLOMERULONEPHRITIS (GN)

Presentation:

- Proteinuria: (Usually < 2gm/day)
- Hematuria
- Intrinsic AKI - HTN - Edema
- **Urine Microscopy:** Dysmorphic RBCs
- (+/-) WBC Cast and RBC Cast

NOTE: **Biopsy** is required for definitive diagnosis of

Rapid Progressive Glomerulonephritis (RBGN):

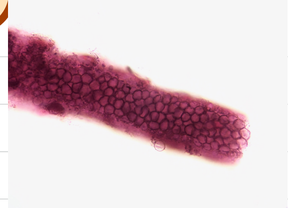
- The most Aggressive Histological pattern of GN
- Acute GN with Rapidly worsening eGFR
- Kidney Biopsy: Glomerular Crescents inside bowman capsule

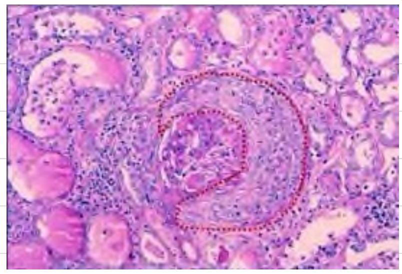
Workup

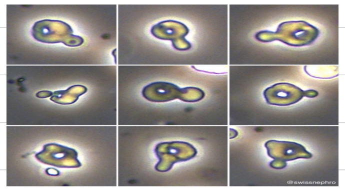
Urine Microscopy and Sediment
ANCA, Anti dsDNA, Anti GBM antibodies, HBV, HCV, HIV
C3/C4, SPEP, Serum Free Light Chain, ASO titer, Blood Cultures

CAUSES of RBGN:

1) Anti GBM antibodies
2) ANCA Associated GN
3) IgA Nephropathy
4) Lupus Nephritis
5) Immune complex MPGN
6) IRGN







INFECTION RELATED GN

Granular deposition in Immunofluorescence

- Previously known as Postinfecious GN and Poststreptococcal GN
- Seen after Group A beta Hemolytic Streptococal infection
- Seen also with Staphylococcus / Endocarditis / Atrioventricular shunt infection

Presentation: 1-6 weeks after the initial illness

- Hematuria
- Edema
- Elevated serum Creatinine

Findings:

- Low Complement level for 6 to 8 weeks after infection
- Low C3 Level only with Endocarditis
- Positive Antistreptococcal Antibody titer
- Elevated Antistreptolysin O Titer (ASO Titer)
- Renal Biopsy: Subendothelial and Subepithelia deposition (Humps appearance)

Treatment:

- Most patients with supportive care and Antibiotics to the underlying infection

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS (MPGN)

COMPLEMENT MEDIATED MPGN:

- Immune Fluorescence is positive for Complement but negative for Immunoglobulin
- due to Dysregulation of the Alternative Complement pathway by Either:

1) Genetic mutation to complement regulatory proteins
    Rx: Intermittent FFP Infusion
2) Antibodies against Complement regulatory proteins
    Rx: Plasma Exchange / Eculizumab

- Low C4 and C3. → Stays low Indefinitely

IMMUNE COMPLEX MEDIATED MPGN:

- Immune Fluorescence is Positive for Complement (C3) and Immunoglobulin
- Usually due to Underlying Systemic Disease:

A) Chronic Infection:
  - Hepatitis (HCV > HBV)
  - NOTE: Hepatitis C is the most common Cause
  - Shunt nephritis
  - Abscess

B) Cryoglobulinemia:
  - Can be Caused by Hepatitis C
    Rx: Steroids, Plasmapheresis, Rituximab / Cyclophosphamide

C) Autoimmune
  - SLE
  - Sjogren Syndrome

D) Monoclonal Gammopathy

Can Present as both Nephrotic and nephritis Syndromes

TREATMENT

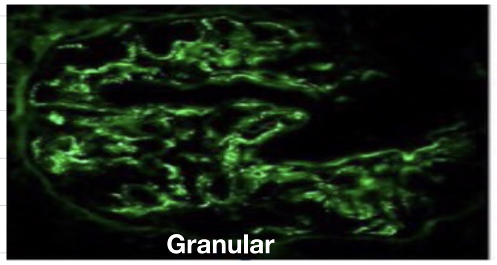
- Treat the underlying disease

LUPUS NEPHRITIS

GRANULAR IF
LOW COMPLEMENT LEVEL

Low C3/C4

Normal C3/C4



IGA NEPHROPATHIES

Granular Immunofluorescence

IgA Nephropathy:

- Most common GN Worldwide
- Occur During or Immediately following an URTI or after Strenuous exercise

Presentation:

- Gross hemturia
- Microscopic Hematuria
- (+/-) Proteinuria

2ry IgA Nephropathy:

- Illnesses Associated with Mesangial IgA deposition but without Glomerular injury
- HIV/AIDS
- Celiac Disease
- End Stage Liver Disease

Findings:

- Normal Complement Level
- Renal Biopsy: Mesangial proliferation and IgA Granular deposits on light microscopy

Treatment

- ACEs/ARBs : for Proteinuria > 0.5g/day
- Steroids: for Persistent Proteinuria > 1gm/day

IgA Vasculitis: (Henoch Schonelin Purapura)

- IgA Nephropathy with Systemic Manifestation

Presentation:

- Abdominal Pain
- Joint Pain
- Lower extremity Palpable Rash
- Hematuria

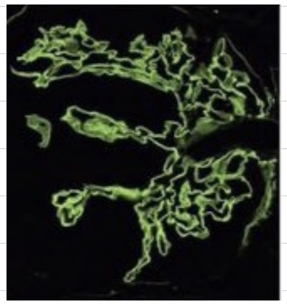
Diagnosis:

- Clinical or by Kidney/Rash Biopsy

Treat suspected RPGN Empirically with
high dose methylprednisolone while waiting for kidney biopsy Results

ANTI-GBM DISEASES

(Linear Deposition on Immunofluorescence)



1) Goodpasture Syndrome:

- With Pulmonary Hemorrhage
- Present with Hemoptysis / Dyspnea
- More common in younger Male patients

2) Anti Glomerular Basement Membrane:

- Renal limited, No Pulmonary hemorrhage
- More common in Older Females

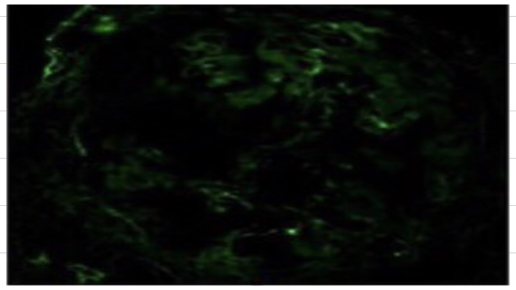
Findings:

- Normal Complement Level
- Renal Biopsy: Linear IgG Deposits along the GBM on IF

Treatment:

- Plasmapharesis
- Steroids + Cyclophsphamide

(ANCA) ASSOCIATED VASCULITIS



(Pauci-Immune)

- Can Cause Crescentic RBGN

1) Granulomatosis with Polyangitis: (Wegner's Granulomatosis)

- Granulomas
- Upper Respiratory Disease (Sinusitis / Epistaxis)
- Lower Respiratory Disease (Hemoptysis/ Cavitary lesions/ Diffuse Alveolar Hemorrhage)
- C ANCA Positive (Anti PR3 [Proteinase 3] Positive)

2) Microscopic Polyangitis:

- Necrotizing Vasculitis but no Granulomas
- Lower Respiratory Disease (Diffuse alveolar hemorrhage)
- Mononeuritis Multiplex (Peripheral neuropathy / Numbness)
- Small Vessel Vasculitis (Palpable Purapura)
- P ANCA Positive (Anti Myeloperoxidase [MPO] Positive)

3) Eosinophilic Granulomatosis Polyangitis: (Churg Strauss Syndrome)

- Asthma/Atopy
- Rhinitis
- Mononeuritis Multiplex (Peripheral neuropathy / Numbness)
- Eosinophilia
- Rash (Purapura)
- P ANCA Positive (Anti Myeloperoxidase [MPO] Positive)

Findings:

- Normal Complement Level
- Positive ANCA
- Kidney Biopsy: Crescentic GN, Negative Immunofluorescence

Treatment:

- Methyelprednisolone + Cyclophosphamide/Rituximab
- Plasmapheresis (for Pulmonary Hemorrhage)

TABLE 12.7. The Glomerulonephritides

DISEASE	PRESENTATION	DIAGNOSIS	TREATMENT
IMMUNE COMPLEX GLOMERULONEPHRITIS			
SLE	Any of the criteria for SLE (see Rheumatology chapter) Lupus nephritis can be the presenting feature	Anti-dsDNA, anti-Sm antibodies ⊕	**Biopsy is essential for staging** Steroids and cyclophosphamide or mycophenolate depending on severity End-stage renal disease (ESRD) occurs in 8%-15% of cases
Postinfectious	**Occurs 2-3 weeks after pharyngitis or skin infection** Classically seen with streptococcal infection, but may be triggered by others	↑ ASO and anti-DNase B antibodies ⊕ ↓ Complement	Treat with diuretics Give antibiotics if infection is still present Renal failure typically resolves in 6 weeks
MPGN	**Cryoglobulin-related MPGN: Arthralgias, palpable purpura, history of HCV infection** Microscopic hematuria with mild to heavy proteinuria May be chronic or rapidly progressive	⊕ cryoglobulins, RF Check HBV, HCV, and HIV serologies Low C3, C4	Treat HCV-related disease and cryoglobulinemia with α-interferon alone or in combination with ribavirin (if kidney function is not severely impaired)
IgA nephropathy	More common in **Asians** and Hispanics Episodic hematuria with or without proteinuria **(usually within 24 hours of URI)** May be primary or secondary to HIV, cirrhosis, IBD, celiac disease	Renal biopsy **Normal C3**	**Mild disease: ACEIs/ARBs** **Progressive disease: Corticosteroids** ± **cyclophosphamide** Ten to 20% of cases progress to ESRD ↑ creatinine, proteinuria, HTN worsens the prognosis
Endocarditis	Episodic hematuria with or without proteinuria	Blood cultures, echocardiography Low C3, C4	Antibiotics The general rule is that if endocarditis is cured, renal impairment will be cured
PAUCI-IMMUNE/ANCA-POSITIVE GLOMERULONEPHRITIS			
Granulomatosis with polyangiitis (formerly Wegener granulomatosis)	**Upper respiratory tract disease and nodular cutaneous lesions are common** Rapidly progressive glomerulonephritis (RPGN)	c-ANCA and anti-PR3 antibody ⊕ Renal biopsy	Steroids with PO cyclophosphamide **Plasmapheresis in cases of pulmonary hemorrhage**
Microscopic polyangiitis	Lower rate of upper respiratory tract than granulomatosis with polyangiitis RPGN	p-ANCA and anti-MPO antibody ⊕ Renal biopsy	Steroids with PO cyclophosphamide
Eosinophilic granulomatosis with polyangiitis (formerly Churg-Strauss syndrome)	**Asthma, allergic rhinitis, eosinophilia** Peripheral neuropathy (mononeuritis multiplex) common	p-ANCA and anti-MPO antibody ⊕ Renal biopsy	Steroids with PO cyclophosphamide
ANTI-GBM GLOMERULONEPHRITIS			
Anti-GBM disease (formerly Goodpasture syndrome)	RPGN May have pulmonary alveolar hemorrhage; dyspnea, cough May have ANCA-associated vasculitis	Anti-GBM antibody ⊕ Renal biopsy	Corticosteroids + cyclophosphamide Plasmapheresis

1.A 43-year-old man comes to the physician because of weakness and arthralgias for the last four months. He also has a pruritic rash on his legs that appeared two months ago. He denies fever or chills and his weight has been stable.

His blood pressure is 140/90 mm Hg and pulse is 84/min. A rash is present on both lower extremities below the knees that consist of many erythematous macules. Laboratory results are as follows:

Complete blood count	
Hematocrit	34%
Platelets	140,000 cells/µL
Leukocyte count	3,000 cells/µL
Serum chemistry	
Creatinine	1.7 mg/dL
Albumin	3.1 g/dL
Aspartate aminotransferase	78 U/L
Alanine aminotransferase	99 U/L
Urinalysis	
Protein	+3
Blood	moderate
Red blood cells	20-30/hpf
Immunologic studies	
Complement	
C3	50 mg/dL
C4	10 mg/dL (12-75 mg/dL)
Rheumatoid factor	90 U/mL (< 40 U/mL)
HIV Antibody	Negative

Which of the following would be most helpful in establishing the diagnosis in this patient?

A. Anti-phospholipid antibodies

B. Bone marrow biopsy

C. Serum protein electrophoresis

D. Urine toxicology screen

E. Viral hepatitis serologies

2. A 40-year-old man seeks evaluation for edema. Two days ago, he had sudden onset of swelling in his legs. There was no associated warmth, redness, or tenderness. The patient had a mild cold a week ago and was taking over-the-counter cold remedies. He thought the swelling was an allergic reaction that would go away, but it has not. His past medical history is unremarkable. The patient does not use tobacco, alcohol, or illicit drugs. He takes no prescription or over-the-counter medications. There is no family history of kidney disease.

The patient's temperature is 36.7 C (98.1 F), blood pressure is 120/70 mm Hg, and pulse is 78/min. He has 3+ pitting edema to the mid-thigh bilaterally. Otherwise, his physical examination is unremarkable.

Laboratory results are as follows:

Hematocrit	42%
Leukocytes	6,900/mm3
Serum chemistry panel	
Sodium	140 mEq/L
Potassium	3.8 mEq/L
Chloride	102 mEq/L
Bicarbonate	26 mEq/L
Blood glucose	100 mg/dL
Albumin	1.9 g/dL
Total cholesterol	420 mg/dL
Urinalysis	
Specific gravity	1.015
pH	5.5
Protein	4+
Blood	Negative
Glucose	Negative
White blood cells	1-2/hpf
Red blood cells	1-2/hpf
Casts	None
Crystals	None

Which of the following diagnoses is most likely to be made with renal biopsy?

A. Allergic interstitial nephritis

B. IgA nephropathy

C. Membranoproliferative glomerulonephritis

D. Minimal change disease

E. Postinfectious glomerulonephritis

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Alanine aminotransferase	99 U/L
Urinalysis	
Protein	+3
Blood	moderate
Red blood cells	20-30/hpf
Immunologic studies	
Complement	
C3	50 mg/dL
C4	10 mg/dL (12-75 mg/dL)
Rheumatoid factor	90 U/mL (< 40 U/mL)
HIV Antibody	Negative

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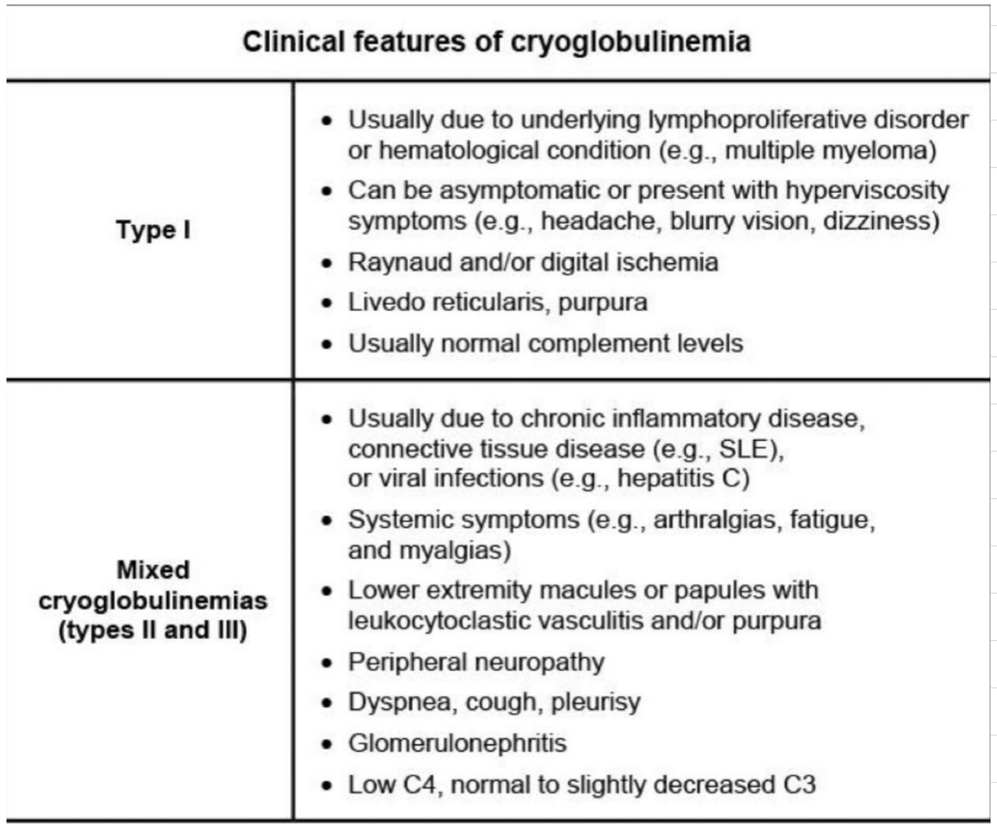

Clinical features of cryoglobulinemia	
Type I	• Usually due to underlying lymphoproliferative disorder or hematological condition (e.g., multiple myeloma) • Can be asymptomatic or present with hyperviscosity symptoms (e.g., headache, blurry vision, dizziness) • Raynaud and/or digital ischemia • Livedo reticularis, purpura • Usually normal complement levels
Mixed cryoglobulinemias (types II and III)	• Usually due to chronic inflammatory disease, connective tissue disease (e.g., SLE), or viral infections (e.g., hepatitis C) • Systemic symptoms (e.g., arthralgias, fatigue, and myalgias) • Lower extremity macules or papules with leukocytoclastic vasculitis and/or purpura • Peripheral neuropathy • Dyspnea, cough, pleurisy • Glomerulonephritis • Low C4, normal to slightly decreased C3

2. A 40-year-old man seeks evaluation for edema. Two days ago, he had sudden onset of swelling in his legs. There was no associated warmth, redness, or tenderness. The patient had a mild cold a week ago and was taking over-the-counter cold remedies. He thought the swelling was an allergic reaction that would go away, but it has not. His past medical history is unremarkable. The patient does not use tobacco, alcohol, or illicit drugs. He takes no prescription or over-the-counter medications. There is no family history of kidney disease.

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Chloride	102 mEq/L
Bicarbonate	26 mEq/L
Blood glucose	100 mg/dL
Albumin	1.9 g/dL
Total cholesterol	420 mg/dL
Urinalysis	
Specific gravity	1.015
pH	5.5
Protein	4+
Blood	Negative
Glucose	Negative
White blood cells	1-2/hpf
Red blood cells	1-2/hpf
Casts	None
Crystals	None

Which of the following diagnoses is most likely to be made with renal biopsy?

A. Allergic interstitial nephritis

B. IgA nephropathy

C. Membranoproliferative glomerulonephritis

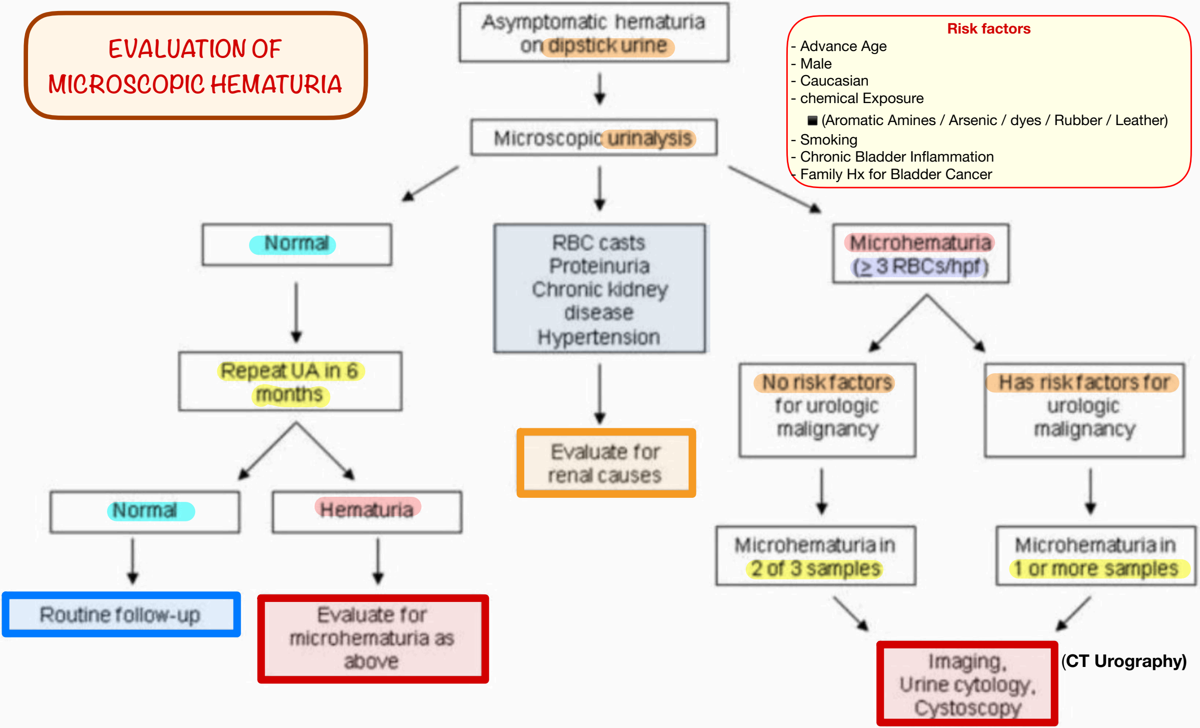
D. Minimal change disease

E. Postinfectious glomerulonephritis

EVALUATION OF MICROSCOPIC HEMATURIA

Risk factors

- Advance Age
- Male
- Caucasian
- chemical Exposure
  - (Aromatic Amines / Arsenic / dyes / Rubber / Leather)
- Smoking
- Chronic Bladder Inflammation
- Family Hx for Bladder Cancer



Asymptomatic hematuria on dipstick urine

Microscopic urinalysis

Normal

Repeat UA in 6 months

Normal

Routine follow-up

Hematuria

Evaluate for microhematuria as above

RBC casts
Proteinuria
Chronic kidney disease
Hypertension

Evaluate for renal causes

Microhematuria (≥ 3 RBCs/hpf)

No risk factors for urologic malignancy

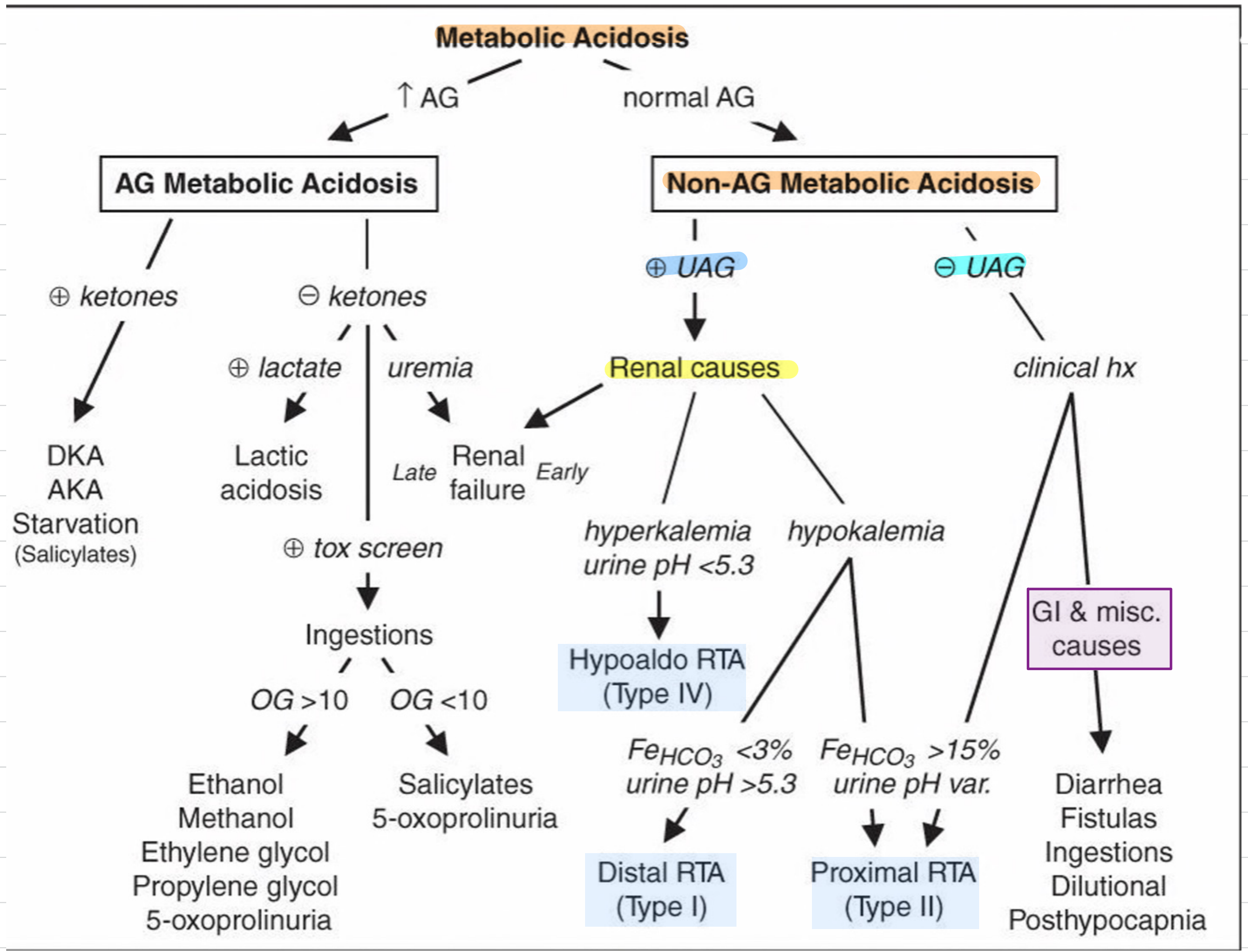
Microhematuria in 2 of 3 samples

Has risk factors for urologic malignancy

Microhematuria in 1 or more samples

Imaging, Urine cytology, Cystoscopy

(CT Urography)



UAG = (urine NA + urine K) - urine CL

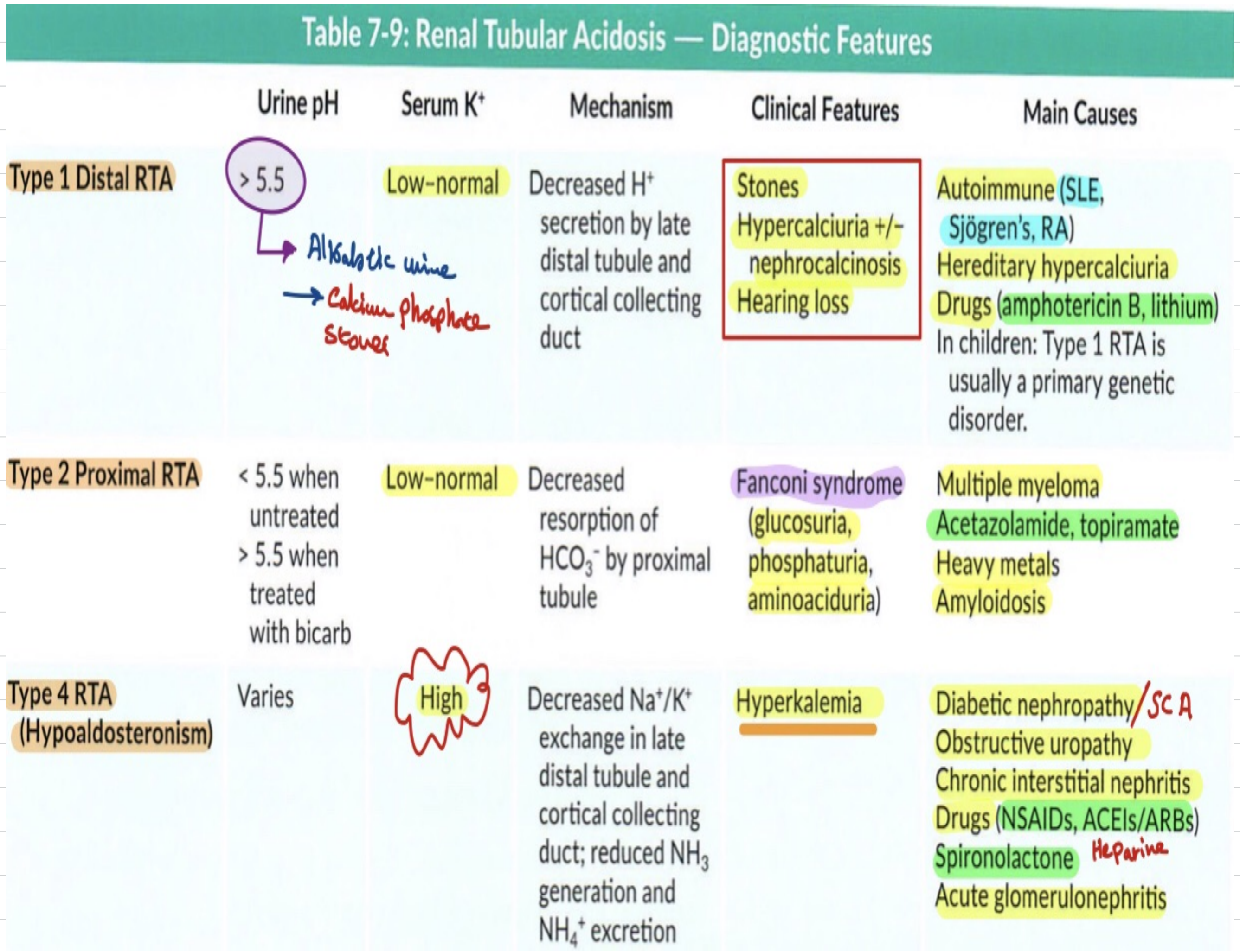
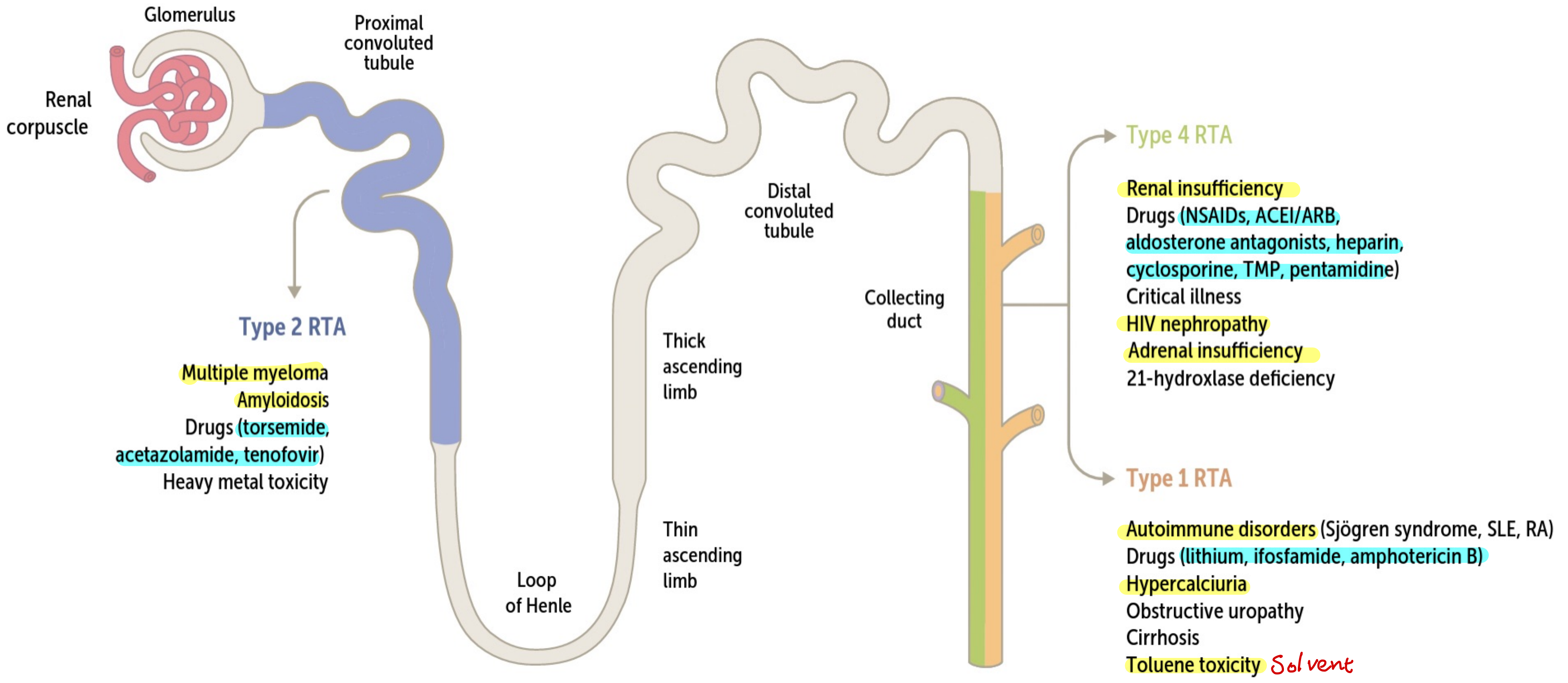


Table 7-9: Renal Tubular Acidosis — Diagnostic Features

	Urine pH	Serum K$^+$	Mechanism	Clinical Features	Main Causes
Type 1 Distal RTA	> 5.5 Alkalotic urine → Calcium phosphate stones	Low-normal	Decreased H$^+$ secretion by late distal tubule and cortical collecting duct	Stones Hypercalciuria +/- nephrocalcinosis Hearing loss	Autoimmune (SLE, Sjögren's, RA) Hereditary hypercalciuria Drugs (amphotericin B, lithium) In children: Type 1 RTA is usually a primary genetic disorder.
Type 2 Proximal RTA	< 5.5 when untreated > 5.5 when treated with bicarb	Low-normal	Decreased resorption of HCO$_3^-$ by proximal tubule	Fanconi syndrome (glucosuria, phosphaturia, aminoaciduria)	Multiple myeloma Acetazolamide, topiramate Heavy metals Amyloidosis
Type 4 RTA (Hypoaldosteronism)	Varies	High	Decreased Na$^+$/K$^+$ exchange in late distal tubule and cortical collecting duct; reduced NH$_3$ generation and NH$_4^+$ excretion	Hyperkalemia	Diabetic nephropathy/SCA Obstructive uropathy Chronic interstitial nephritis Drugs (NSAIDs, ACEIs/ARBs) Spironolactone Heparine Acute glomerulonephritis



Type 2 RTA

Multiple myeloma
Amyloidosis
Drugs (torsemide, acetazolamide, tenofovir)
Heavy metal toxicity

Type 4 RTA

Renal insufficiency
Drugs (NSAIDs, ACEI/ARB, aldosterone antagonists, heparin, cyclosporine, TMP, pentamidine)
Critical illness
HIV nephropathy
Adrenal insufficiency
21-hydroxlase deficiency

Type 1 RTA

Autoimmune disorders (Sjögren syndrome, SLE, RA)
Drugs (lithium, ifosfamide, amphotericin B)
Hypercalciuria
Obstructive uropathy
Cirrhosis
Toluene toxicity Solvent

E.

Toxic alcohols		
Toxicity	**Clinical features**	**Laboratory results**
Alcohol ketoacidosis	- Slurred speech - Unsteady gait - Altered mentation	- High osmolar gap - Increased anion gap metabolic acidosis (ketosis)
Methanol ingestion Rx: - Fomebizole (Preferred) - Ethanol	- Visual blurring, central scotomata - Afferent pupillary defect - Altered mentation	- High osmolar gap - Increased anion gap metabolic acidosis
Ethylene glycol ingestion	- Flank pain - Hematuria, oliguria - Cranial nerve palsies, tetany	- High osmolar gap - Increased anion gap metabolic acidosis - **Calcium oxalate crystals** in urine
Isopropyl alcohol ingestion	- CNS depression - Disconjugate gaze - Absent ciliary reflex	- High osmolar gap - **No** increased anion gap or metabolic acidosis

CNS = central nervous system.

1. An 18-year-old male has been brought to the emergency department for altered mental status. His friends report that he was at a party when he became incoherent and developed slurred speech, so they called 911. No other history is available.

On examination, he is drowsy and has slurred speech. His temperature is 36.7 C (98 F), blood pressure is 90/60 mm Hg, pulse is 96/min and respirations are 22/min. No focal neurologic findings are present and the general physical examination is unremarkable.

The patient's labs reveal:

Complete blood count	
Hematocrit	38%
Leukocyte count	8,000/mm3
Serum chemistry panel	
Sodium	140 mEq/L
Potassium	5.2 mEq/L
Chloride	98 mEq/L
Bicarbonate	14 mEq/L
Blood urea nitrogen (BUN)	10 mg/dL
Creatinine	1.0 mg/dL
Calcium	9.6 mg/dL
Blood glucose	100 mg/dL
Blood ethanol	10 mg/dL
Osmolality	312 mg/dL
ABG	
pH	7.25
PO2	100 mm Hg
PCO2	23 mm Hg
Urinalysis	
Specific gravity	1.020
Blood	negative
Glucose	negative
Ketones	negative
Leukocyte Esterase	negative
Nitrites	negative
WBC	1-2/hpf
RBC	1-2/hpf
Casts	none

Serum Osmolarity?
AG?
Urine AG?

Which of the following is the most likely cause of this patient's illness?

A. Isopropyl alcohol ingestion

B. Ketoacidosis

C. Lactic acidosis

D. Methanol ingestion

E. Salicylate ingestion

3. A 70-year-old woman presents to the emergency department because of anorexia, nausea, and diarrhea. She has had these symptoms for the past 3 days. She recently completed a course of antibiotics for bronchitis. Her medical problems include osteoporosis, type 2 diabetes mellitus, hypertension, glaucoma, and osteoarthritis. Her current medications include metformin, fosinopril, chlorthalidone, ibandronate, acetazolamide, and acetaminophen. Her temperature is 37.4°C (99.4°F), blood pressure is 120/70 mm Hg, pulse is 84/min, and respirations are 16/min. On examination, she appears uncomfortable. Her abdomen is mildly tender in both of the lower quadrants. Test of the stool for blood is positive. The patient's laboratory studies reveal:

Hematocrit	38%
Platelet count	350,000/mm3
Leukocyte count	15,000/mm3
Serum sodium	136 mEq/L
Serum potassium	3.8 mEq/L
Chloride	116 mEq/L
Bicarbonate	12 mEq/L
Serum creatinine	1.4 mg/dL
Blood glucose	160 mg/dL
ABG	
pH	7.26
PO2	85 mm Hg
PCO2	31 mm Hg
Urine	
Chloride	84 mEq/L
Potassium	20 mEq/L
Sodium	28 mEq/L

Which of the following is responsible for this patient's acid-base disorder?

A. Acetazolamide

B. Fosinopril

C. Gastrointestinal losses

D. Metformin

E. Type 4 renal tubular acidosis

5. A 70-year-old woman is admitted to the hospital with a fractured hip after a fall.

Laboratory results are as follows:

Serum chemistry	
Sodium	136 mEq/L
Potassium	3.6 mEq/L
Chloride	110 mEq/L
Bicarbonate	15 mEq/L
Creatinine	0.8 mg/dL
Arterial blood gases	
pH	7.3
PO2	104 mm Hg
PCO2	34 mm Hg

Which of the following medications is most likely responsible for her acid-base abnormality?

A. Acetazolamide

B. Mesalamine

C. Metformin

D. Omeprazole

E. Zoledronic acid

---

4. A 67-year-old man with chronic obstructive pulmonary disease (COPD) is seen in the emergency department for increasing dyspnea. His most recent FEV1 was 0.8 L and he is on chronic oxygen therapy. Two days ago, he began coughing up increased sputum and felt more short of breath. One day ago, he noticed that his sputum became purulent and his shortness of breath worsened. He denies chest pain, hemoptysis, fever, abdominal pain, or nausea. He receives an annual influenza vaccination and obtained vaccination for *S. pneumoniae* three years ago. He denies any other new symptoms and does not have diarrhea, nausea, or vomiting. He has hypertension, hyperlipidemia, and type 2 diabetes mellitus. His current medications include albuterol, tiotropium, lovastatin, hydrochlorothiazide, and metformin.

On examination, he appears dyspneic. His temperature is 36.7 C (98 F), blood pressure is 130/90 mm Hg, pulse is 96 /min, and respirations are 20 /min. He has difficulty speaking in complete sentences. There is no asterixis. Cardiac examination demonstrates a right ventricular lift, but is otherwise normal. All breath sounds are decreased. There is prolongation of the expiratory phase of respiration. There are no rales or rhonchi. Abdominal examination is normal. Extremity examination shows 1+ pedal edema bilaterally to the mid-shin.

Fingerstick blood glucose is 90 mg/dL. A metabolic panel shows that his serum creatinine is 1.0 mg/dL.

Which of the following arterial blood gases (ABG) would be most compatible with his clinical picture?

A. pH 7.30, bicarbonate 34 mEq/L, and anion gap of 8 mEq/L

B. pH 7.30, bicarbonate 24 mEq/L, and anion gap of 10 mEq/L

C. pH 7.30, bicarbonate 14 mEq/L, and anion gap of 17 mEq/L

D. pH 7.47, bicarbonate 24 mEq/L, and anion gap of 10 mEq/L

E. pH 7.47, bicarbonate 34 mEq/L, and anion gap of 8 mEq/L

RENAL STONES

TABLE 12.3. Types, Mechanisms, and Treatment of Kidney Stones

TYPE	MECHANISMS AND DISEASE ASSOCIATIONS	TREATMENT[a]	NOTES
Calcium oxalate Calcium phosphate	**Hypercalciuria:** Hyperparathyroidism, malignancy, granulomatous diseases **Hyperoxaluria:** Short gut syndrome, IBD **Hypocitraturia:** Metabolic acidosis from RTA, CKD, chronic diarrhea	**Ca^{++} restriction is not helpful** (may lead to hyperoxaluria) important Thiazides, potassium citrate **Low Na^+ diet** Remember Citrate = Good Oxalate = Bad	Citrate is the 1° stone formation inhibitor **Vitamin C:** is an Oxalate, and if taken in large amounts can cause Ca Oxalate Stones
Uric acid	**Acidic urine (pH <5.5):** A diet high in animal protein **Hyperuricosuria:** Gout, tumor lysis syndrome	**Allopurinol, potassium citrate to alkalinize urine**	
Cystine	**Hypercystinuria:** Cystinuria	Tiopronin (Thiola)	
Struvite Triple phosphate Staghorn calculi	**Alkaline urine (pH >6.5):** UTI with urease-splitting organisms (eg, *Proteus mirabilis*)	Treat the underlying infection Stone Removal / surgical Intervention	Recurrent UTIs may be due to a residual nidus of infection from the stone
Medication-related	Triamterene, acyclovir, indinavir, methotrexate		

[a] In addition to large-volume water intake.

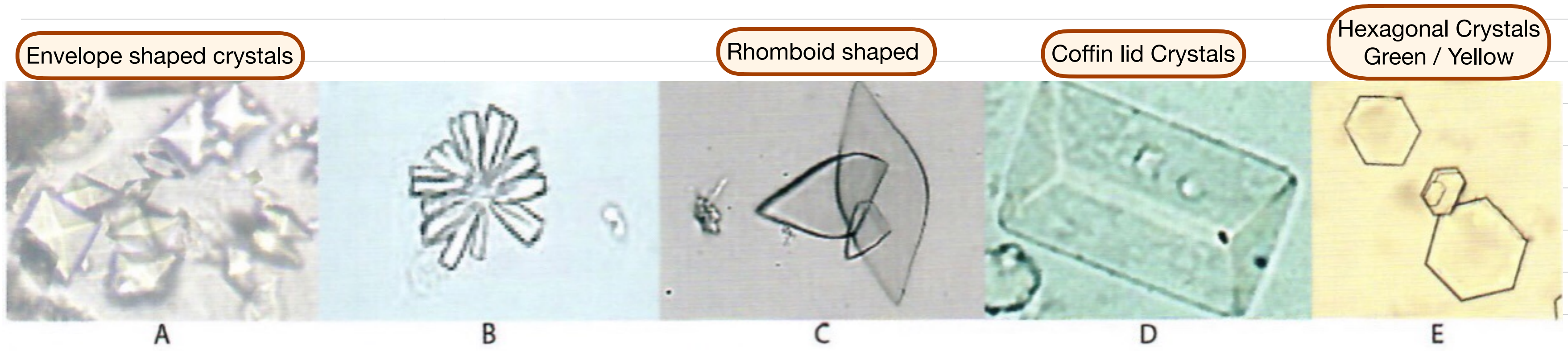


Figure 7-2: Urine sediment: Crystals. (A) Calcium oxalate. (B) Calcium phosphate. (C) Uric acid. (D) Struvite. (E) Cystine.

RENAL IMAGING

1) CT Abdomen & Pelvis W/O Contrast

- **Gold Standard &. Test of Choice**

2) Renal U/S

- 1st Choice In Pregnant Women

MANAGEMENT

- **Pain Control:** NSAIDs & Opioids if Needed
- Hydration & α-Blockers (Tamsulosin) Can Facilitate Stone Passage
  - NOTE: Stones > 1cm Ususally doen not Pass and Need Urologist Intervention
- **Hospitalization if:**
  - Evidence of Infection (Leukocytosis / Fever)
  - Obstruction (Hydronephrosis on Imaging)
  - AKI

2. A 36-year-old woman comes to the office because of recurrent dysuria. She also complains of dull pain in her right flank, blood in her urine, and cloudy urine. She has a history of recurrent urinary tract infections since she became sexually active in high school. She has had three episodes of urinary tract infections over the last year accompanied by fever. Her last urine culture grew *Klebsiella pneumoniae*. She has been in a monogamous relationship and uses a diaphragm (or her partner uses a condom), both with spermicidal coatings for contraception.

Her temperature is 38.1 C (100.5 F), blood pressure is 114/70 mm Hg, and pulse is 95/min. Abdomen is soft and non-tender. She has mild bilateral costovertebral angle tenderness to percussion.

Complete blood count	
Hematocrit	34%
Leukocyte count	13,000 cells/µL
Serum chemistry	
Sodium	140 mEq/L
Potassium	4.2 mEq/L
Chloride	102 mEq/L
Bicarbonate	24 mEq/L
Creatinine	1.9 mg/dL
Uric acid	8.0 mg/dL
Urinalysis	
Specific gravity	1.013
pH	8.0
Protein	none
Blood	moderate
Glucose	negative
Leukocyte esterase	positive
Nitrites	positive
Bacteria	many
White blood cells	20-30/hpf
Red blood cells	20-30/hpf

Which of the following is the best treatment for this patient's condition?

A. Discontinuation of spermicides

B. High-volume fluid intake and allopurinol

C. Post-coital antibiotic prophylaxis

D. Stone removal procedure

E. Urinary acidification

1. A 45-year-old man is evaluated for recurrent urolithiasis. He underwent a Roux-en-Y procedure for morbid obesity two years ago. He passed his first kidney stone one year ago and has passed several since then. He has lost approximately 15 kg (33 lb) since the surgery and feels well otherwise. His current medications include lisinopril for hypertension, esomeprazole for gastro-esophageal reflux disease, and a daily multivitamin. He has no family history of kidney stones.

Which of the following factors is most likely responsible for this patient's kidney stone formation?

A. High urinary oxalate and low urinary citrate

B. Hypercalciuria

C. Hyperuricosuria and low urine pH

D. Low urinary volume

E. Vitamin D deficiency

CHRONIC KIDNEY DISEASE

INTRODUCTION

- Definition:

1) Kidney damage > 3 Months
  - Albuminuria
  - Active Urine Sediment
  - Abnormal Imaging (Cystic Kidney / Hydronephrosis)
  - Abnormal Pathology

2) GFR < 60 (with or without Kidney Damage)

- Stages:
- Stage 1: GFR > 90
- Stage 2:GFR 60-89
- Stage 3a: GFR 45-59
- Stage 3b: GFR 30-44
- Stage 4: GFR 15-29 (Prepare for Renal Replacement Therapy)
- Stage 5: GFR < 15

- DM Is the Most Common Cause, Followed by HTN
- Proteinuria is the Most Important Predictor of Progression of Renal Disease
- Heart Disease is the Number 1 Cause of Death in CKD
- Screen ALL CKD Patients for Hepatitis C and treat if Positive

UREMIA

Signs and Symptoms of Uremia (*NEJM* 2018;379:669)	
General	Nausea, anorexia, malaise, uremic fetor, metallic taste, hypothermia
Skin	Uremic frost (white crystals in & on skin), pruritus, calciphylaxis
Neurologic	Encephalopathy (Δ MS, ↓ memory & attention), seizures, neuropathy, impaired sleep, restless leg syndrome
Cardiovascular	Pericarditis, atherosclerosis, HTN, CHF, cardiomyopathy (LVH)
Hematologic	Anemia, bleeding (due to platelet dysfunction and Epo deficiency)
Metabolic	↑ K, ↑ PO_4, acidosis, ↓ Ca, 2° hyperparathyroidism, osteodystrophy

SLOW PROGRESSION

1) Smoke Cessation

2) BP Control:
- Target BP < 130/80 (Decrease Mortality)
- ACE/ARB: (Check Creatinine in 1-2 weeks and d/c if Increased 30%)

3) Glycemic Control:
- Optimize Glycemic Control (HgbA1c < 7%)
- Treat Albuminuria (with or without HTN) with ACE/ARB
- SGLT2 Inhibitors Reduce Risk of CKD Progression (in Pt with GFR ≥ 30%)

4) Dyslipidemia
- Target LDL < 100 mg/dl
- treat with Statin or Statin/ezetimibe combination
- Do not Initiate Statins in Patients with ESRD who are on Dialysis (no benefit)
- In patients with High Triglycerides, Treat with Lifestyle Modificati
- Avoid Fibrates (Risk for Rhabdomyolysis)

5) Dietary Modification
- Lower Protein Intake to 0.8g/kg/day
- Low Protein Diet to < 0.6g/kg/day is Not Recommended
- Sodium Restriction to < 2g/day Improves BP and Volume Overload
- If Hyperphosphatemia, Restrict Dietary Phosphate to 900mg/Day
- Low Potassium Diet

6) Avoid Nephrotoxins
- Iodine Contrast
  - Hydration with Isotonic Saline Infusion
  - Hold ACE/ARBS & Other Nephrotoxins Agesnts
- NSAIDS
- Aminglycosides

COMPLICATION

1) Metabolic Acidosis:
- Treat with Sodium Bicarbonate

2) Uremic Pericarditis:
- **Hemodialysis**

3) Peritoneal Catheter Associated Peritonitis
- Cloudy Fluid / Fever / Abdominal Pain
- S aureus, Staphylococcus epidermidis, gram-negative rods, and fungi
- Diagnose with
  - Gram stain
  - >100 WBCs/μL in peritoneal fluid
  - Culture of peritoneal fluid
- Treat with antibiotic infusion into the peritoneum

4) Anemia of CKD
- Target Hgb 10-11.5
- **Increase Mortality if Hgb > 12**
- Iron supplementation Before Starting Erythropiotin if
  - ◆ Transferrin Saturation < 30%
  - ◆ ferritin < 500
- Trial of Oral Iron with CKD Patient NOT on Dialysis, if not Improved then IV
- IV Iron for Patients on Hemodialysis
- If Hgb not Improved after Proper Replacement, Then Erythropiotin

5) Bleeding (Uremic Plt Dysfunction)
- Treat with Desmopressin
- Estrogen Is 2nd Line
- in Severe Bleeding Do Platelets / Cryoprecipitate transfusion

6) Hyperkalemia
- Dietary Restriction
- Calcium Gluconate
- Insulin / Salbutamol
- Calcium Resonium

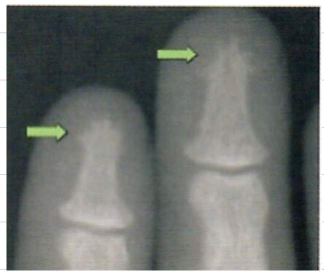
7) CKD-MBD (Develop Due to 2ry Hyperparathyroidism)

↑ Phosphate
↓ Calcium
↓ Vitamin D

- Maintain Ca & Ph Levels Close to The Normal Range
- Screen All CKD Pt for Vitamin D Deficiency
- Rx Hyperphospgatemia with Diet restriction & Phosphate Binders
- **Phosphate Binders**
  - Calcium Based (calcium Ca & Ca Acetate)
    - ◆ *Avoid in Hypercalcemia Calcium*
    - ◆ *They Can Cause Vascular Calcification & worsen MBD*
  - Non-Calcium Based (Sevelamer & Lanthanum)
  - Aluminum Containing Phosphate Binders
    - ◆ *Cause Dementia and the should not be used*

8) 2ry Hyperparathyroidism
- Target PTH 2-9 X the Upper limits *(To Prevent Adynamic Bone Disease)*
- Use Active Vit D Analogue
  - Calcitirol / Dpxercalciferol
  - Ued in Hypocalcemia
- Cacimimetics (Cinacalcet) can also be used
  - Should be Limited to A Ptient on Hemodialysis
  - Used in Normal / High Calcium

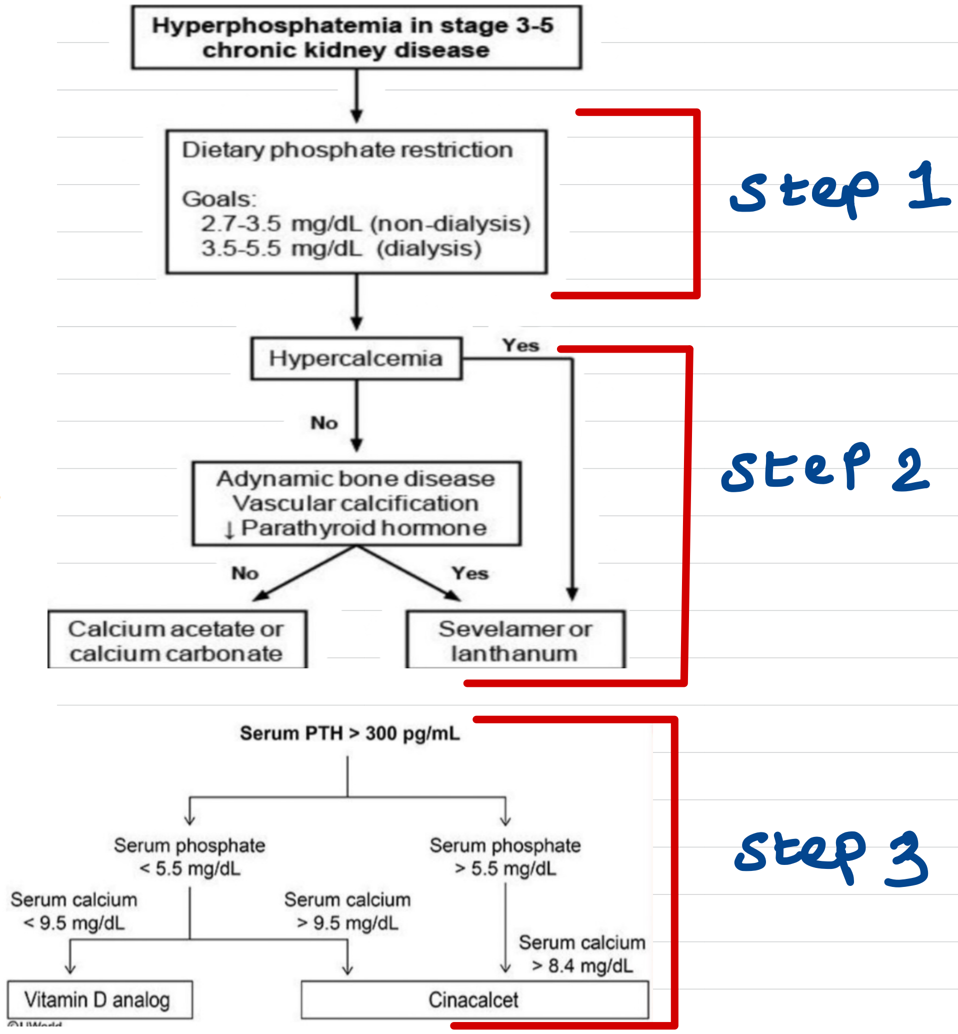
9) Renal OsteoDystrophy



A) Osteitis Fibrosa Cystiica
- High turnover Bone disease
- From Persistent 2ry Hyperparathyroidism
- Develop Bone Pain & Fractures
- High Alkaline Phosphatase Levels
- **CXR:** Subperiosteal Bone Resorption
- Rx: Treat CKD-MBD

B) Adynamic Bone disease
- Low Bone Turnover State
- Caused by Oversuppression of PTH from Over treatment of CKD-MBD
- Alkaline Phosphatase Levels are Normal
- PTH Levels are Low (<100)
- Bone Biopsy is the Gold Standard for Diagnosis (Rarely Needed)
- Rx:
  - Reduce / Stop Vitamin D
  - Stop / Change Calcium Based Phosphate Binders

C) Osteomalacia
- Now Rare in CKD
- Was Due the Use of Aluminum Containing Phosphate Binders


Hyperphosphatemia in stage 3-5 chronic kidney disease
Dietary phosphate restriction
Goals:
2.7-3.5 mg/dL (non-dialysis)
3.5-5.5 mg/dL (dialysis)
step 1
Hypercalcemia
Yes
No
Adynamic bone disease
Vascular calcification
↓ Parathyroid hormone
No
Yes
Calcium acetate or calcium carbonate
Sevelamer or lanthanum
step 2
Serum PTH > 300 pg/mL
Serum phosphate < 5.5 mg/dL
Serum phosphate > 5.5 mg/dL
Serum calcium < 9.5 mg/dL
Serum calcium > 9.5 mg/dL
Serum calcium > 8.4 mg/dL
Vitamin D analog
Cinacalcet
step 3

8. A 55-year-old man comes to the physician for follow-up of chronic kidney disease. He feels well overall and has no acute problems. His medical problems include type 2 diabetes mellitus, hypertension, obesity, and hyperlipidemia. His medications include furosemide, simvastatin, low-dose aspirin, amlodipine, and glipizide. Physical examination is normal with +2 peripheral pulses in all extremities.

Laboratory results are as follows:

Serum chemistry	
Sodium	136 mEq/L
Potassium	4.4 mEq/L
Chloride	102 mEq/L
Bicarbonate	22 mEq/L
Creatinine	3.0 mg/dL
Calcium	8.0 mg/dL
Glucose	120 mg/dL
Blood, plasma, and serum	
Albumin	3.7 g/dL
Phosphorus, inorganic	6.0 mg/dL
Parathyroid hormone	200 pg/mL

In addition to a phosphate-restricted diet, which of the following would be the preferred therapeutic option?

A. 1,25 dihydroxyvitamin D

B. Aluminum hydroxide

C. Calcium acetate

D. Lanthanum

E. Sevelamer

HEREDITARY KIDNEY DISEASES

POLYCYSTIC KIDNEY DISEASE

TYPES

A) *AUTOSOMAL DOMINANT*
- The Most Common Genetic Disease of the Kidney
- Ptient develop cysts in Kidneys / Liver / Pancreas
- Eventually Develops ESRD
- **Diagnosis:** Imaging (CT or U/S) >> Polycystic kidneys
- **Screening:** U/S for Pt > 18 years with Family Hx of PKD

B) *AUTOSOMAL RECESSIVE*
- Less Common
- Present with Renal Failure and Hepatic Fibrosis in infancy and Early Adulthood

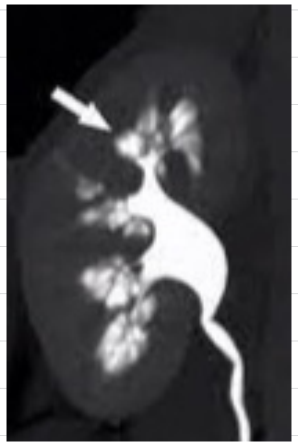
PRESENTATION

- Gross Hematuria (Most Common)
- Microscopic Hematuria
- Flank Pain
- HTN
- Cysts Infections
- Hepatomegaly (Liver Cysts)
- Valvular Heart Disease (MVP is the Most Common)
- **Cerebral Aneurysm**
    - ◆ Screen if family Hx of Subarachnoid hemorrhage or Cerebral Aneurysm

TREATMENT

- Supportive
- Tight Blood Pressure Control
- Tolvaptan (Monitor LFT)
- Infected Cysts: Antibiotics for 2-4 Weeks

MEDULLARY SPONGE KIDNEY



INTRODUCTION

- Generally Benign

PRESENTATION

- Hematuria
- Renal Stones (Calcium Phosphate)
- Recurrent UTI

DIAGNOSIS

A) Intravenous Pyelogram IVP
- Bouquet of Flowers 💐 Appearance

B) U/S or CT
- Medullary Nephrocalcinosis

THIN BASEMENT MEMBRANE DISEASE

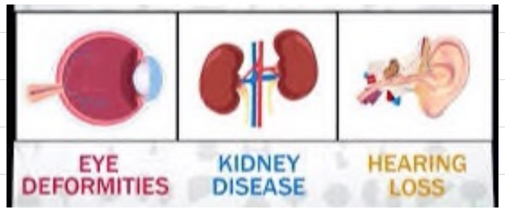
- Benign Disease
- Present with Isolated Microscopic Hematuria
- Biopsy: Thin GBM

ALPORT SYNDROME

INTRODUCTION

- Also Known as Hereditary Nephritis
- Can be either (X linked / AD / AR)
- Mutation in the type 4 collagen Affecting the Basement Membrane
    - ◆ Glomerulus
    - ◆ Cochlea
    - ◆ Lens

PRESENTATION



- Hematuria & Proteinuria
- CKD
- Deafness
- Ocular Defects

DIAGNOSIS

- Biopsy
    - # Thickened GBM
    - # Splitting of the Lamina Densa >> **Hallmark of the disease**

TREATMENT:

- Kidney Transplantation

(Pt can develop Anti-GBM disease after transplantation because of the exposure to Normal type 4 collagen)

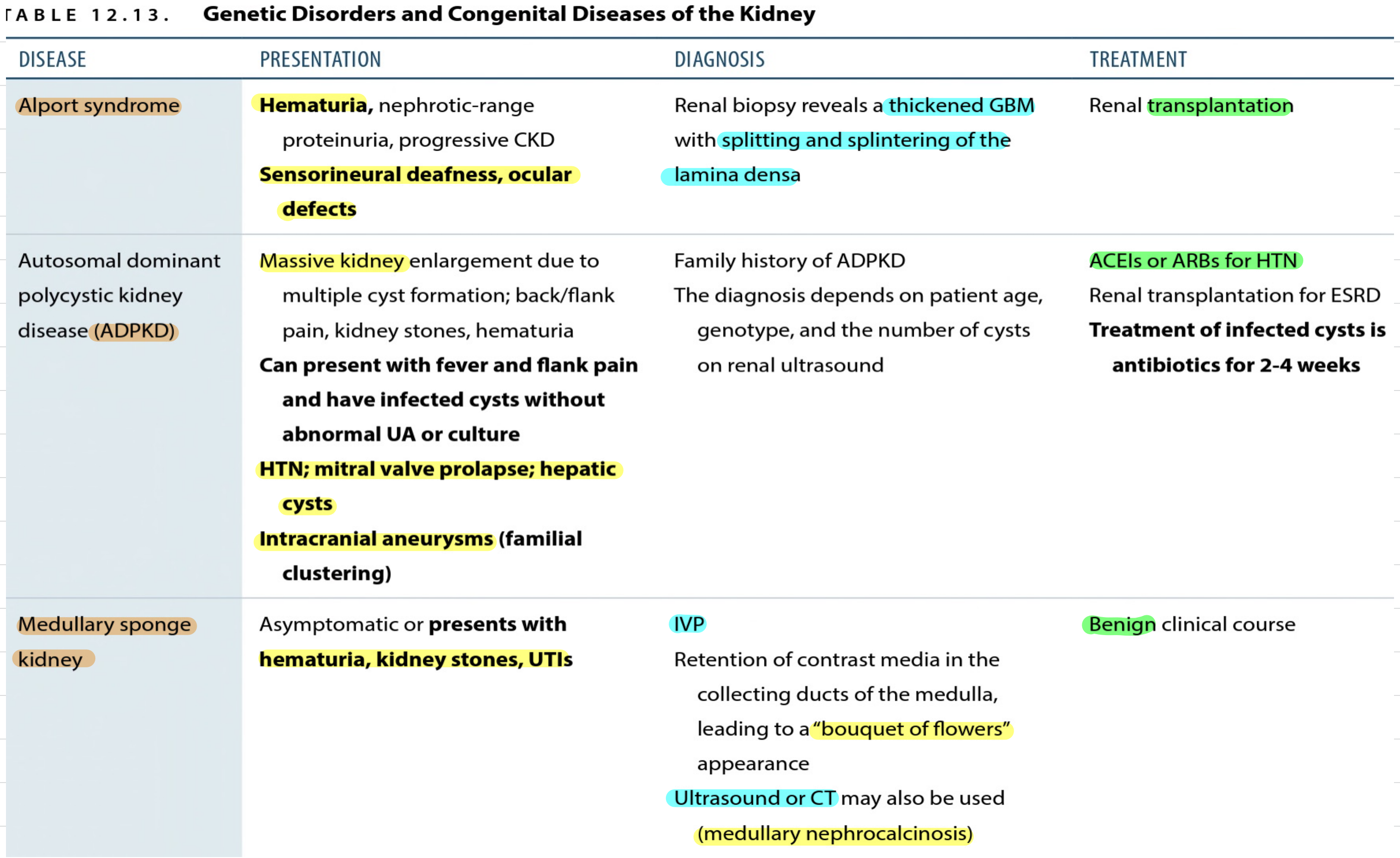


TABLE 12.13. **Genetic Disorders and Congenital Diseases of the Kidney**

DISEASE	PRESENTATION	DIAGNOSIS	TREATMENT
Alport syndrome	**Hematuria,** nephrotic-range proteinuria, progressive CKD **Sensorineural deafness, ocular defects**	Renal biopsy reveals a thickened GBM with splitting and splintering of the lamina densa	Renal transplantation
Autosomal dominant polycystic kidney disease (ADPKD)	Massive kidney enlargement due to multiple cyst formation; back/flank pain, kidney stones, hematuria **Can present with fever and flank pain and have infected cysts without abnormal UA or culture** **HTN; mitral valve prolapse; hepatic cysts** **Intracranial aneurysms (familial clustering)**	Family history of ADPKD The diagnosis depends on patient age, genotype, and the number of cysts on renal ultrasound	ACEIs or ARBs for HTN Renal transplantation for ESRD **Treatment of infected cysts is antibiotics for 2-4 weeks**
Medullary sponge kidney	Asymptomatic or **presents with hematuria, kidney stones, UTIs**	IVP Retention of contrast media in the collecting ducts of the medulla, leading to a "bouquet of flowers" appearance Ultrasound or CT may also be used (medullary nephrocalcinosis)	Benign clinical course